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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,521	SCHREIBER, GIDEON	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62, 66-71, and 75- 86* is/are pending in the application.

4a) Of the above claim(s) *84 and 86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62, 66-71, 75-83 and 85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response of May 30, 2006, to the non-final action dated November 21, 2005 has been entered. Claims 62 and 75 have been amended; claims 63-65 have been cancelled by the Applicant in the paper dated May 30, 2006. Claims 72-74 were cancelled in the paper dated March 21, 2006. Claims 62, 66-71, and 75- 86 are pending in the application. Claims 84 and 86 remain withdrawn from consideration, with traverse. This application contains claims 84 and 86 drawn to an invention nonelected with traverse in the paper filed on November 21, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 62, 66-71, 75-83 and 85 are under current examination.

Priority

Acknowledgment is made of receipt for applicant's foreign priority document, based on an application filed in Israel on December 31, 2001.

Failure to Comply with Nucleotide and /or Amino Acid Sequence Disclosures 37CFR§1.821-1.825

37 CFR§1.821 (d) states: Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Figure 2 depicts the amino acid sequence of the wild type human IFNAR2 EC (extracellular) domain. Neither Figure 2, nor the description of the figure (paragraph [0026], p. 7), refer to the sequence as SEQ ID NO: 1. Applicant is required to check both the as filed paper and CRF sequence listings to ensure concordance with the sequence depicted in Figure 2. The instant application may be placed in compliance with 37 CFR 1.821-1.825 by amending either the Figure or the brief description of the Figure to refer to SEQ ID NO: 1.

Claim Objections

Amended claim 62 is objected to because of the following informalities: the claim recites "said mutation". As the claim refers to two separate mutations, the claim should recite "said mutations. Appropriate correction is required.

Amended claim 75 is objected to because of the following informalities: the claim is directed to the polypeptide according to any one of claims 62-71. As claims 63-65 have been cancelled, the claim should recite any one of claims 62 or 66-71. Appropriate correction is required.

Response to Claim Rejections - 35 USC § 101

Claims 62-65, and 67-74 were previously rejected in the office action of November 21, 2005, under 35 USC §101, as directed to non-statutory subject matter.

Applicant disagrees with the Examiner's finding, stating that the Examiner has misapplied the statutory subject matter requirement. In view of Applicant's amendment of base claim 62 to recite "an isolated IFNAR2 polypeptide", and the cancellation of claims 63-65 and 72-74, the previous rejection of the claims is rendered moot and is therefore withdrawn.

Claim Rejections - 35 USC § 112, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 62, 67-71, 75-83 and 85 stand rejected in modified form under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art (hereafter the Artisan), that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims read on any alternative receptor form of IFNAR2 polypeptide from numerous species of animals that expresses an endogenous beta chain subunit of the type I IFN receptor (e.g. membrane bound and cytoplasmic forms). As such, the claims encompass a multitude of membrane bound, cytoplasmic or soluble forms of IFNAR2 polypeptides that may be isolated and mutated from numerous species of animals. The specification discloses the human form of IFNAR2 extracellular domain (identified in Figure 2 and SEQ ID NO: 1), that are mutated at positions His 78 and Asp 100, and designated IFNAR2-EC (Example 2). However, the specification provides no cross-species analysis to demonstrate that such receptors from other species were included in the present invention. The claims encompass a large number of receptor sub-type sequences that contain IFN-β binding activity and genes encoding IFNAR2 in different species of animals. The claims thus constitute a claimed genus that encompasses other polypeptide and genomic sequences that may encode an IFNAR2 receptor, yet to be discovered, and since the specification only discloses a single species (a **human** IFNAR2- **EC** polypeptide, as in SEQ ID NO:1 and Figure 2), the disclosed structural features of said receptor do not constitute a substantial portion of the claimed genus. As such, the Artisan of skill could not predict that Applicant possessed any additional species, except for the human IFNAR2-EC receptor. Hence, only the polypeptide sequence from the human IFNAR2 extracellular portion could be demonstrated as possessed.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). Moreover, MPEP 2163 states:

> [A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Applicant's attention is also directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Overall, what these statements indicate is that the Applicant must provide adequate description of such core structure and function related to that core structure such that the Artisan of skill could determine the desired effect. Hence, the analysis above demonstrates that Applicant has not determined the core structure for full scope of the claimed genus.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. Therefore, the breadth of the claims as reading on IFNAR2 receptor sequences yet to be discovered; in view of the level of knowledge or skill in the art at the time of the invention, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of the genus of IFNAR2 sequences containing alternatively spliced forms of the receptor in numerous animal species (Claim 62). Thus it is concluded that the written description requirement is not satisfied for the claimed genus. Claims 63-65, 67-71, 75-80, 82-83 and 85 depend from claim 62.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of membrane bound or other soluble forms of IFNAR2 polypeptides that may be isolated and mutated from any species of animal; at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Response to Claim Rejections - 35 USC § 112, Written Description

Claims 62-65, 67-83 and 85 were previously rejected under 35 U.S.C. §112, first paragraph, in the office action of November 21, 2005, as failing to comply with the written description requirement.

Applicant's cancellation of claims 63-65 and 72-74, and the amendment of claims 62 and 75, directing the claims to individual species explicitly described in the application as originally filed, only partially obviates the rejection of the claims, as additional deficiencies relating to the written description remain in the claims. For example, the instant specification provides written description support of a human IFNAR2 EC polypeptide. Hence, possession at the time of the invention could be demonstrated only for the extracellular form of the human IFNAR2 receptor, not alternatively spliced membrane bound or cytoplasmic forms of IFNAR from human or other species of animals, that are encompassed by base claim 62.Applicant has not provided any specific arguments to the aforementioned issues, also raised in the previous office action. Therefore, the rejection is maintained for reasons of record and the discussion set forth above.

Response to Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 62, 66-71, and 75-82 stand rejected under 35 U.S.C. §112, first paragraph, for lacking an enablement for the full scope of the invention. The rejection set forth on pp. 5-9 of the previous office action dated November 21, 2005 is maintained for claims 62, 66-71, and 75-82 for reasons of record.

Applicant's amendment of the claims to be directed to individual elected species explicitly described in the application, fails to obviate the rejection, because the claims still broadly encompass isolated and mutated polypeptide sequences of numerous receptor variants of the type I IFN receptors, such as membrane bound, cytoplasmic or soluble forms, that may be present in any species of animal. Applicant has not provided any specific arguments to the aforementioned issues, also raised in the previous office action.

Therefore, it is maintained that the specification is only enabling for an isolated **human** IFNAR2- **EC** polypeptide, comprising SEQ ID NO:1, wherein amino acid residues His 78 and

Asp 100 of the extracellular domain are substituted by alanine, as set forth in SEQ ID NO: 2.

Response to Claim Rejections - 35 USC § 112-Lack of Enablement

Claims 83 and 85 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The rejection set forth on pp. 9-10 of the previous office action dated November 21, 2005 is maintained for reasons of record.

Applicant disagrees with one of the issues raised in support of the rejection, arguing: "selecting the appropriate effective amount of a composition for a particular patient is well within the skill of the ordinary artisan and may be determined without undue experimentation. Applicant's argument has been fully considered, but not found to be persuasive.

As was indicated on page 9 of the first office action, the prior art teaches that the role and contribution of IFNAR2, to ligand binding and signal transduction remains unknown, and that soluble IFNAR2a has been found to inhibit the functional activity of type I interferon. Further, the instant specification discloses that the advantages of using mutated IFNAR2EC are that it is possible to administer lower quantities of the receptor as a carrier and because of the stabilizing activity of the mutant, it is possible to reduce the amount of IFNβ administered. However, the specification also teaches that "in some inflammatory disorders, where it may be required to lower the IFN concentrations, it is possible under certain conditions to use this mutant as an effective antagonist specifically toward IFNβ" (p. 9, paragraph 0035). The specification fails to provide a description of what constitutes a therapeutically effective amount of a composition comprising the IFNAR2 mutated polypeptide and optionally an IFN antagonist, as recited in claims 83, and how an Artisan would differentiate between said therapeutic amount serving as a carrier for IFN versus an antagonist for IFN. The specification also fails to provide any description wherein said composition has been administered to a patient having an autoimmune disorder or multiple sclerosis, either alone or in combination with IFN. Therefore, the reference to "therapeutic amount" is in context of the different properties (i.e. as protagonist and antagonist) attributable to an IFNAR2 mutant polypeptide.

Applicant has failed to address the foregoing issues and the points raised in the first office action. Thus, the rejection of claims 83 and 85 is maintained for reasons of record and the discussion set forth above.

Response to Claim Rejections - 35 USC § 103

Claims 62, 66-71 and 75-76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Piehler et al. (of record). The rejection set forth on pp. 10-11 of the previous office action dated November 21, 2005 is maintained for claims 62, 66-71, and 75-76 for reasons of record.

Applicant disagrees with the rejection, stating that the Examiner has failed to consider evidence of secondary considerations, such as unexpected results. Specifically, that the claimed double mutants cause a synergistic effect on the affinity of the polypeptide to IFNβ compared to a single mutations at positions H78 and N100. Applicant's arguments have been fully considered, but are not found persuasive.

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding **unexpected results**, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP § 716.01(c), II. and § 2145.

Moreover, as was indicated on p. 11 of the previous office action, Piehler et al. specifically describe the mutant H78A as stabilizing the complex with IFN-β nearly two fold; the mutation N100A decreasing dissociation rate constant for IFNβ by almost fourfold; and further stating: "It would be interesting to explore the phenotype of a H78, N100 double mutation in ifnar2, which should have about a 20-fold tighter binding for IFNβ". Thus, Piehler expected a synergistic effect for the double mutation.

Therefore, the rejection of claims 62, 66-71 and 75-76 is maintained for reasons of record and the foregoing discussion.

Claims 77-81 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Piehler et al. (of record), in view of Campbell et al. (of record). The rejection set forth on pp. 11-12 of the previous office action dated November 21, 2005 is maintained for claims 77-81 for reasons of record.

Applicant disagrees with the rejection, citing the deficiency of Piehler et al. indicated for claims 62, 66-71 and 75-76 above. Such is not found persuasive, in view of reasons of record and the discussion set forth above. Therefore, the rejection of claims 77-81 is maintained.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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PRIMARY EXAMINER